AN EXPLORATORY ANALYSIS OF MORTALITY AMONG EMPLOYEES OF CELANESE CANADA INC. KINGSTON (MILLHAVEN), ONTARIO

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EXECUTIVE SUMMARY

In April 1989, the Health Studies Service of the Ministry of Labour (MOL) through the Health and Safety Support Services Branch, was informed of concerns about cancer occurrence in the HDI (Heavy Decitex Industrial or Tire Yarn) area among employees of Celanese Canada Inc, in Millhaven, Ontario. Apparently these concerns were first communicated to the Kingston office of MOL by two former employees with kidney and lung cancers. In May 1989, a meeting took place with representatives of management, the union, the Joint Health and Safety Committee (JHSC), and the Ministry of Labour. Although no specific type of cancer was mentioned as being of concern, the anxiety focussed on the HDI area and exposure to the compound known as phenyl glycidyl ether (PGE or C-8).

It was agreed at the meeting that the Ministry of Labour would undertake an exploratory study to examine if the cancer experience of Celanese Canada employees differed from that of the Ontario population, and that the quickest method would be an analysis of deaths available from company files. During the discussion, it was pointed out in some detail the limitations in trying to determine whether a problem was present at the plant in general (and the HDI department in particular) because 1) the HDI plant had only started operation in the 1960s while it generally takes 20 years or more for occupationally-induced cancer to appear; and 2) there would only be small numbers of deaths available for analysis. According to information from Human Resources staff at the plant, the HDI department comprised only about 111 employees in 1966/67, 195 in 1976/77, and 99 in 1986/87 which represented between 9 to 19% of plant personnel over time, and is therefore quite small relative to the total plant population (workforce).

A mortality study of polyester workers reported from France (Hours et al, 1986) suggested that there were excess deaths from lung and laryngeal cancers (the latter statistically

significant). However, the process in this French plant was somewhat different from that in the HDI plant. Excess deaths due to kidney cancer were not reported. No known human carcinogens are present in the HDI process. However, PGE is mutagenic and has induced nasal cancers in animals. Dimethyl terephthalate, the main raw material used in the polyester process, was not considered carcinogenic in an animal feeding study but a dose-related increase in primary lung tumours was observed in male mice which may have been associated with long-term administration of the compound.

The method used for the study at Celanese Canada involved proportional mortality which is convenient for exploratory analysis because it is based on data provided from the company's pension, mortality, and insurance records; and avoids having to trace workers who terminated employment after shorter periods. The study examined mortality patterns among ever-payroll employees dying while active, retired, or on long-term disability. The Human Resources and Public Relations staff provided a listing of deceased payroll and staff employees, and work histories with most but not all change of jobs indicated by rate or transfer slips and termination slips.

Of the 132 names supplied, 115 were ever in payroll, and for 108, employment status at death was known to be active, retired, or long-term disability. Death certificates were obtained for 103 and cause of death was known from insurance records for two others (these were not from cancer). Of these 105 deaths, 88 were in males and 17 were in females.

The initial analysis found that, compared to the general population of Ontario, the proportions of deaths from all cancers were about that expected. For lung cancer, the proportions were slightly above that expected among both retirees and those dying while active. No deaths from kidney cancers or nasal cancers were observed.

The next phase of the analysis examined mortality experience according to work area, using the work histories provided. It is recognized that it takes some years for chemically induced tumours to appear; thus, in investigating the relationship between chemical exposures in the workplace and cancer deaths, it is reasonable to assume that work exposures in the years shortly before death are unlikely to have caused tumours. Thus, jobs performed within five years of death were not considered.

Of the 105 employees, 11 (10.4%) had ever worked in the HDI area while 94 had not. In comparison with the general population of Ontario, the proportion of deaths due to all cancers was increased among ever HDI workers (6 observed vs 3.7 expected) while the proportion in the never HDI workers was the same as expected. The only case of laryngeal cancer occurred in an HDI worker. Lung cancer was the only cancer for which there was more than one case among HDI workers; there was no evidence of increased deaths from other causes of cancer among HDI workers. There were 3 lung cancers (0.88 expected) in males and females combined; two of the four deaths in HDI women were lung cancer (0.4 expected); this 3-fold excess of deaths due to lung cancer was not statistically significantly different from that expected. Among the non-HDI workers, the numbers of observed lung cancers was slightly greater than expected; a subset analysis after examining the jobs showed this to be limited to those in maintenance jobs but the incomplete nature of the work histories prohibited further examination of non-HDI deaths.

Other causes of lung cancer, such as smoking, could explain the increase in lung cancers among HDI employees if smoking habits were different in these workers than in the general population. No data are available to examine this; however, no deaths from respiratory diseases (chronic bronchitis, emphysema) or bladder cancer, both of which are known to be smoking-related, occurred among HDI workers (rather, they were found only among non-HDI workers).

The three HDI lung cancer deaths were found only among those 45-64 years of age. In this subgroup, the proportion of deaths due to lung cancer was 38% among HDI and 15% among non-HDI; the crude odds ratio for the association of lung cancer and work in HDI (summing both sexes) was 3.5 and the Mantel-Haenszel summary odds ratio (adjusting for sex) was 4.1 ($p=0.35$), which is not statistically significant. That is, lung cancer appeared about three to four times more frequently among HDI workers, but this could be due to chance.

All three cases worked for only a short duration of time in HDI (0.4, 0.4, and 3.8 years, respectively, prior to 5 years before death). Work for prolonged periods in other departments in common was not identified, and one death occurred less than 10 years since first exposure in the HDI area. No deaths occurred after more than 20 years since first in HDI, which is not surprising as the HDI plant began operations in the 1960s. The 2 women were 54 and 55 years of age at death. There is no evidence for increased deaths from other cancer causes in HDI.

In summary, a "cluster" of lung cancer deaths has been identified among HDI workers that was not "statistically significant" based on 3 cases and less than 1 expected. The short duration of work in HDI of these cases argues against the association with HDI department being causal. While it is recognized that this study is limited by not examining incident cancers, because of the short period of follow-up that has elapsed since start of the operation, and the small number of HDI workers (and deaths among HDI workers to date), it is doubtful that at this time, one can obtain a definitive answer to the question of whether lung or other cancer risk among HDI workers is increased.

It is recommended that the mortality experience or cancer incidence be examined among those HDI workers with long duration of exposure and <u>greater than 20 years since first working in HDI</u>, that is, 5-10 years in the future. However, in order to gain more information at the present time, it is <u>preferable</u> to examine

workers exposed to the same process at a <u>different</u> location, to see if the findings, which are only suggestive here and cannot be considered causal, are observed elsewhere. Such a location exists at a Celanese plant in North Carolina which has an HDI process and a larger exposed workforce; a mortality study is already underway at this facility. It is recommended that the JHSC obtain the results of this study when available; the Health Studies Service is eager to assist in interpreting the findings in conjunction with the JHSC.

INTRODUCTION

In April 1989, the Health Studies Service of the Ministry of Labour (MOL), through the Health and Safety Support Services Branch (HSSSB), was informed of concerns about cancer occurrence among employees of Celanese Canada Inc, in Millhaven, Ontario. Apparently, these concerns were first communicated to the Kingston office of the Ministry of Labour (MOL) via two former employees with cancer, one with kidney and one with lung cancer. In response, the HSSSB staff indicated following a March 1989 meeting at the plant that a mortality study would be requested of the Health Studies Service.

On May 15, 1989, a meeting took place with representatives of management, the Joint Health and Safety Committee, union officials, and Ministry of Labour investigators from Health Studies Service and HSSSB. The Health and Safety Committee indicated that some employees were concerned about cancer occurrence at the plant. Although no specific type of cancer was expressed as being of concern, the concerns did focus on the HDI area and exposure to the compound known as C-8 (phenyl glycidyl ether).

It was agreed at the meeting that the Ministry of Labour would undertake an exploratory study to examine if the cancer mortality experience of Celanese Canada employees differed from that of the Ontario population. The most rapid method of doing so would be by performing an analysis of the mortality pattern of the deaths which could be identified from company files.

The author pointed out that there might be some difficulty in trying to determine whether a problem was present at the plant in general (and the HDI department in particular) because: (1) the HDI plant had only started operation in 1966-68 while it generally takes 20 years or more for occupationally-induced cancer to appear; and (2) the small numbers of deaths available

for analysis would limit the investigators' ability to detect problems above random fluctuations in the number of deaths sometimes referred to as background "noise" in the data.

PLANT HISTORY

An overview of the plant history and production processes was provided by Dr. Tetlow and staff. The polyester plant opened as CIL operation in 1954-55 (although CIL maintained an ammonia plant on the site previously); the facility has undergone various ownership changes over time, and is currently owned by Celanese Canada. There are a number of different departments: polyester production (filament, staple, tire yarn/HDI), batch polymer plant, production services, as well as rework waste recovery, powerhouse, maintenance, laboratory/ quality control, and warehouse/stores. In addition, nylon was produced from about 1965-70. Figure 1 provided by Dr. Tetlow describes the production department changes over time.

Polyester (a type of synthetic fibre) can be used for a variety of products including textiles and clothes, tire cord and seat belts. The material has been made by several processes at the plant. The basic process (Mattiussi and Armelli, 1983) involves making dimethyl terephthalate react with ethylene glycol in the presence of appropriate catalysts (cobalt or zinc acetate; magnesium, antimony or lead oxides). This yields the interchange ester which is transferred to polymerization autoclaves, where polycondensation occurs and polyethylene terephthalate is formed. Upon reaction completion, the molten polymer is discharged, cooled to promote solidification, and treated to obtain filaments by extrusion.

At Celanese, polyester is produced in the Staple unit (used in polyester clothes); and in the Tire Yarn or Heavy Decitex Industrial Yarn (HDI) unit, where it is used for car tires and

CELANESE CANADA INC. - MILLHAVEN PLANT : PRODUCTION PROCESSES

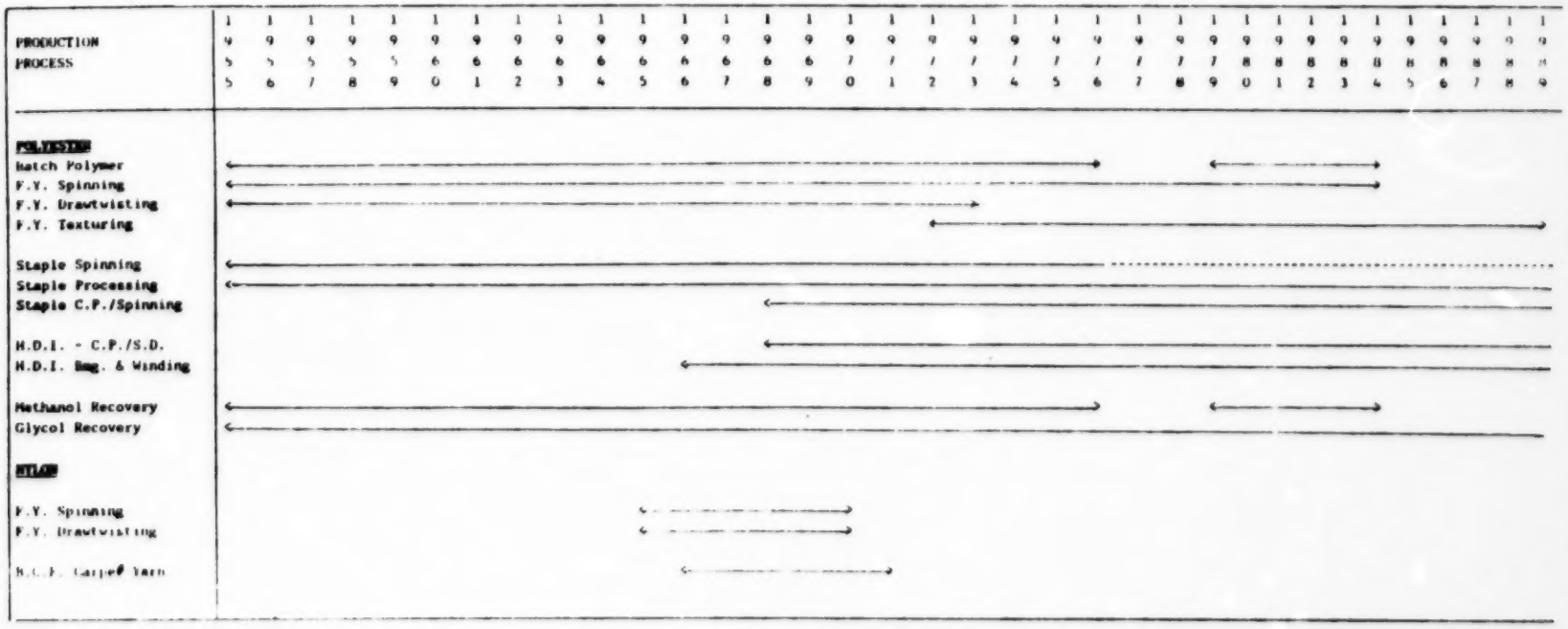

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FIGURE 1

seat belts. Polyester was also made at the batch polymer plant from the time of plant opening in 1955 through 1984 (except 1976-1979), and through Filament Yarn (until about 1985). More details of the HDI process follow below.

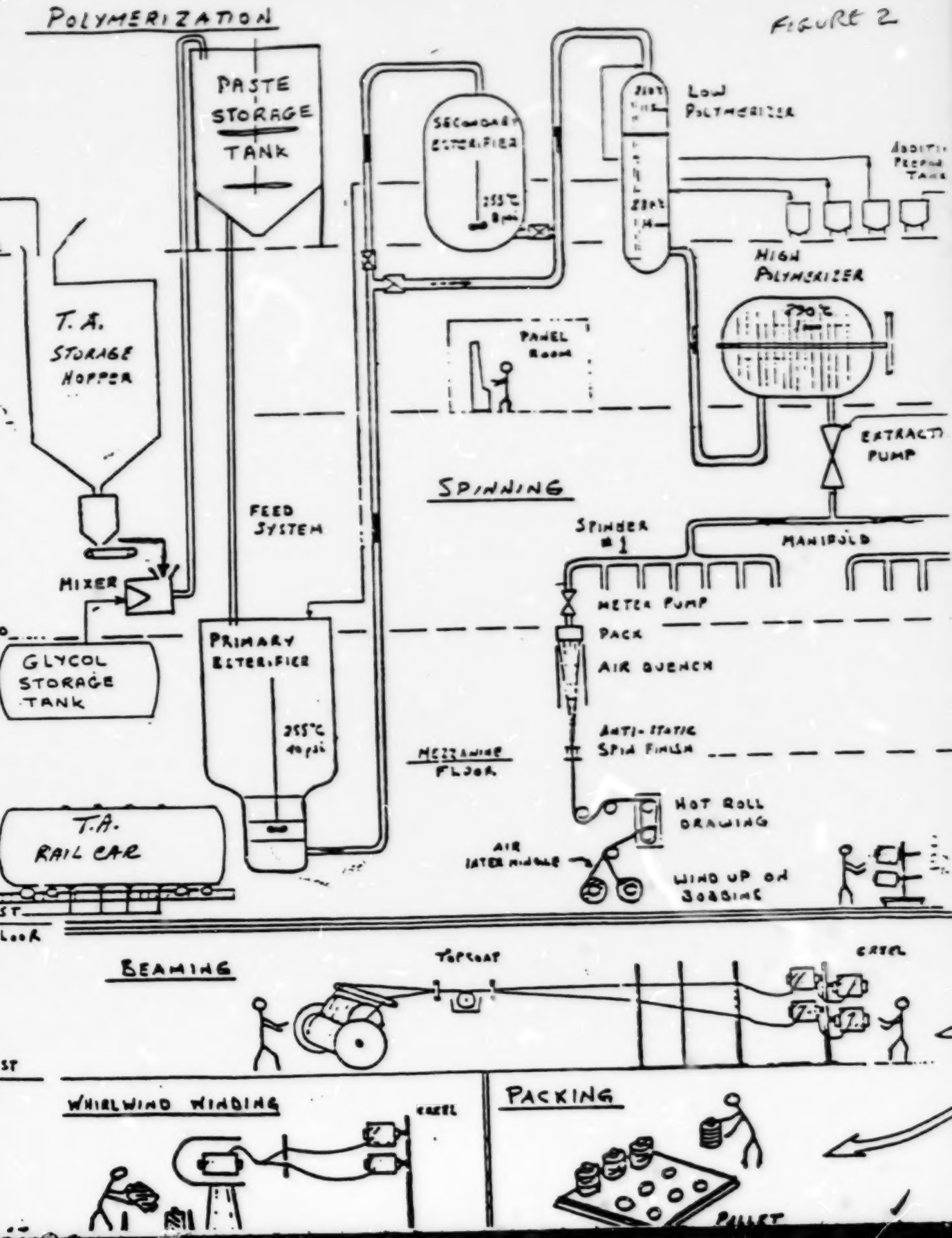
Process description of Heavy Decitex Industrial Yarn (HDI)

The unit has two parts: the continuous polymerization and spin-draw (CP/SP) [polymerization to create the polyester, extrusion, drawdown and heat set] which opened in 1968; and beaming, whirlwind twisting, and packaging operations, which began in 1966.

The process starts (see Figure 2 supplied by Dr. Tetlow) with the raw materials of terephthalic acid and ethylene glycol, mixed in proportions of 1.4:1 mole ratio, pumped to the first reaction vessel (primary esterifier), where the mixture is subjected to heat and pressure, and additives (including choline in methanol, and sodium hydroxide) are added. In the secondary esterifier, the reaction completion increases from 90% to 98%. The monomer is then transferred to polymerization vessels, where antimony oxide catalyst and other additives are introduced. The molten polymer then is prepared to undergo extrusion.

Phenyl glycidyl ether (PGE; C-8) which is pumped from 45-gallon drums to a holding tank, is metered into the molten polymer system. PGE, which was used in the HDI plant in 1972-73 and from 1976 onwards, reacts with the carboxylic end groups of the terephthalic acid. The polymer is then extruded (as fibre). The filaments are quenched and proprietary lubricants, emulsifiers, and anti-static materials are applied. The filament bundle is then drawn over temperature controlled heated rolls (drawn yarn), and then wound onto a cardboard cylinder (winding). At this point the yarn is fully drawn and can be sold as a package or processed further on a textile beamer (beaming) and sold in beamed form, or processed on a Whirlwind winder for sale as a

SCHEMATIC FLOW FOR HEAVY DTEX INDUSTRIAL YARN (H.D.I.) PLANT



twisted product. The packaged material goes to the warehouse.

The major HDI production chemicals are listed below.

CHEMICAL	MSDS#	USAGE (kg/yr)
Antimony trioxide	39	32200
Choline base	424	16100
Proprietary finishes		
Code 142	443	8302
Code 185	451	17562
Code 208	460	83178
Code 227	462	8292
Code 234	463	6232
Phenyl glycidyl ether	2617	18874
Terephthalic acid	3609	44482324
Ethylene glycol	1115	24825348

Reports on Health Hazards of Polyester Production

A review of the materials at the plant by HHHSB indicated no known human carcinogens present. However, little has been published concerning the mortality of workers producing polyester, the main product of Celanese Canada.

One retrospective cohort study from France (Hours et al, 1986) found that among "Tergal" or polyester production workers, there were 6 lung cancer deaths observed vs 3.29 expected (standardized mortality ratio [SMR] 182) (not statistically significant) and a statistically significant increase in laryngeal cancers (4 observed, 1.4 expected, SMR 285, one-sided p=0.05). However, the author of the present report wrote to Dr. Hours who indicated the process was somewhat different from HDI: (1) the products are for textiles; (2) a nickel rather than an antimony oxide catalyst

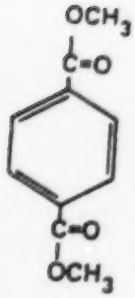
is used; and (3) he was not aware that PGE was present. These French authors were not certain of what might be the carcinogenic agent, if any, but suggested as possibilities the nickel catalyst, coumarins from tars, or phthalates (particularly di(2-ethylhexyl)phthalate, which is not used at Celanese) A recent update of this cohort through 1986 (Hours et al, 1989) again found an excess of lung cancer among tergal (polyester) workers that was not statistically significant. In additional case-control analyses by these authors, there was no relationship of lung cancer risk to duration of employment. Excess deaths due to kidney cancer were not reported.

An animal feeding study of dimethyl terephthalate (the main raw material used in the polyester process; structure shown in Figure 3) (NCI, 1979), a dose-related increase in primary lung tumours observed in male mice may have been associated with long-term dietary administration of dimethyl terephthalate. However, the study concluded that the compound was not considered carcinogenic for F344 rats or B6C3F1 mice.

Phenyl glycidyl ether (PGE) is mutagenic, and induced nasal carcinomas (i.e. site of contact) in Sprague-Dawley rats at 12 ppm but not at 1 ppm (Lee et al, 1983).

Antimony oxide exposure has been associated in one report with an excess of deaths due to lung cancer in workers involved in antimony smelting (in the presence of other contaminants) at an average concentration in air of 8 mg/m^3 (Gudzovskij, 1983). No data were encountered to suggest the compound presents such a hazard among users of antimony.

Dowtherm (diphenyl, diphenyl oxide) functions as a heat-transfer agent in the production process and is the major component of Dowtherm A. It is used in increasing amounts as a chemical intermediate in the production of surface active agents and high-temperature lubricants. Eye and nasal irritation were



Dimethyl terephthalate

FIGURE 3

observed in rats and rabbits (but not dogs) exposed to 10.0 ppm for 7 hr/day, 5 days/wk for 20 exposures, while no signs of toxicity or irritation were observed in animals exposed to 4.9 ppm (Hefner et al, 1975). After a Finnish worker died in 1969 following heavy exposure to diphenyl (biphenyl) for eleven years in a process involving the production of wrapping paper impregnated with the material, a survey of 31 men engaged in the process suggested both central and peripheral neurological lesions (Hakkinen et al, 1973). A detailed description of the neurological changes in the workers at the biphenyl-impregnated paper plant (Seppalainen et al, 1975) suggested that these abnormalities were persistent. There are no data on carcinogenic effects.

T-55: T-55, a proprietary finish used for five years in the spin draw area of Tire Yarn was mutagenic in the Ames assay and produced reproductive changes (decreased testicular weight) on dermal application in high concentrations to male mice (Source: HSSSB file). Its use was discontinued in 1981.

Exposure data

As is customary in occupational mortality studies where the exposures of concern may have occurred 10-20 or more years in the past, quantitative data on the exposures are often missing or sparse. Exposure data were available from two sources:

(1) Air monitoring data carried out by the Company:

(a) PGE: Samples taken in Spin Draw/ HDI, both personal and area, annually from 1980 through 1988, indicated mean values all less than or equal to 1.87 mg/m^3, compared to an allowable time weighted average exposure value of 60 mg/m^3 (through the early 1980s), and 6 mg/m^3 in recent years (ACGIH, 1987). The range of values indicates maximum peak area samples of 3.6 and 3.5 mg/m^3 in 1982 and 1983,

respectively.

(b) Dowtherm: Results taken in 1987 and 1988, in the Spin Draw (area and personal) ranged from <0.1 to 1.4 mg/m^3 compared to the ACGIH TLV of 1.5 mg/m^3 (ACGIH, 1987), set to prevent respiratory difficulties following repeated inhalation exposure at 5 mg/m^3 in the mouse.

(c) Antimony tripxide (Sb_2O_3): Between 1980 and 1988, personal samples obtained in the Spin Draw area, averaged 0.003-0.05 mg/m^3 (range up to 0.12) and area samples averaged 0.001-0.05 mg/m^3 (range up to 0.13), all less than the Time Weighted Average Exposure Value (TWAEV) of 0.5 mg/m^3.

Other compounds: Very low exposures to isopropyl alcohol, 1,1,1-trichloroethane and xylene were also reported.

(2) Air quality assessments carried out in earlier years by the Occupational Health Branch (now HSSSB) of the MOL.

(a) Terephthalic acid: In 1979, results of personal air samples indicated concentrations of 1.4 and 0.9 mg/m^3 for Staple operators, and 1.7 and 0.7 mg/m^3 for Tire Yarn process operators.

(b) Phenyl glycidyl ether: Results of personal air samples (about 2 hours in duration) in Tire Yarn in 1979 demonstrated considerable variation: from 0.09 to 62 ppm (in operators on mezzanine floor, air quench chambers); 3.0 and 139 ppm for additive man (relief man on pack floor); and 0.27 and 1.1 ppm (process operators). Area air samples (about 1-2 hrs in duration) indicated concentrations of 0.26 to 164 ppm in the Mezzanine Floor (air quench chambers); concentrations of 0.65 and 0.54 ppm near PGE injection (pack floor); 0.89 and 94 ppm above metering pumps on 3rd floor; 220 and 0.19 ppm (in the additive room, 5th floor); and < 0.02 ppm in the spin finishing area. These determinations can be compared to the TLV of 10 ppm then in effect. Thus, overexposure to the existing criterion was documented in the late 1970s. The TWAEV has since been reduced to 1 ppm based on studies demonstrating irritation and hair loss (alopecia)

in male and female rats at 12 and 5 ppm (Terrill et al, 1977; 1982)). Although not noted in the ACGIH documentation, nasal tumours were also induced at 12 ppm (Lee et al, 1983).

A comment in a 1979 field report: suggested that attempts be made to lower exposure by giving more attention to preventing leaks in the piping systems containing PGE; and that certain improvements were required to reduce employee exposure in the additive area and the mezzanine floor.

(c) Antimony trioxide: Results of personal samples (15 minutes in length) were 11.3 mg/m^3 for additive man (Tire Yarn), and 106 mg/m^3 for process operator (Staple). Results of area samples (again short term) indicated exposure of 12.0 mg/m^3 above mixing tanks (Tire Yarn Additive Room, 5th floor), and 60.7 mg/m^3 near mixing tank (Staple Additive Room, 3rd floor).

(d) Asbestos: Like most industrial plants, asbestos was and is present in insulation. A 1983 OHB report noted that samples were taken from fixture insulation for chrysotile asbestos analysis. No air sampling results were noted, and no note was made as to whether the insulation was friable. An asbestos control program was developed.

Numbers of employees

Although the plant census has varied with market demand over time, turnover has historically been low. Figures supplied by Dr. Tetlow indicated that the number of hourly payroll and salaried staff was about 400-500 and 200, respectively, in the late 1950s; about 1000-1100 and 300, respectively, in the late 1960s through mid-1970s; about 700 and 170, respectively, in the late 1970s; and about 600 and 150, respectively, in recent years.

Numbers supplied by EC Murray, Human Resources Superintendent, suggested that Tire Yarn employees, as a proportion of the total

plant census, comprised about 111 employees in 1966/67 (approximately 9% of plant); 195 employees in 1976/77 (about 19%); and 99 employees (about 13%) in 1986/87. Therefore, the size of the HDI population available for study is quite limited.

STUDY METHODS

The method used for this study involved Proportional Mortality, based on data provided from the company's pension, mortality, and insurance records. Thus, an existing data source is used, and avoids the much more time-consuming and expensive process of tracing those who have terminated employment after shorter periods. In proportional mortality analysis, the proportions or relative frequency of deaths from various causes in the Celanese study group are compared with the proportions found in the general population of Ontario. Based on the limited literature available, specific comparisons of interest might be the percentages of deaths among Celanese workers compared to that in the population of the same age in Ontario for: lung cancer (suggested by an epidemiologic study, animal bioassay, and by one of the former workers), laryngeal cancer (epidemiologic study), nasal cancer (PGE in animals) and kidney cancer (one of the former workers).

Proportional Mortality Ratios (PMRs) were derived by (see below):

$$PMR = \boxed{\text{observed/ expected} \times 100} \quad \text{where}$$

observed deaths are obtained from company records; and
expected deaths are derived from the Ontario population.

With the ages and dates of deaths for Celanese employees, a computer program (Coleman et al, 1986) was used to calculate the proportions of lung, laryngeal, or other cancers one might expect if the mortality experience of Celanese employees were no

different than that of the Ontario average population.

Study population

The Manager, Human Resources and Public Relations of Celanese Canada and his staff provided a listing of deceased payroll and staff employees obtained from insurance and pension data. The intent was to examine mortality patterns among ever-payroll (hourly) employees dying while active, retiree, or on long-term disability. Of the 41 staff deaths notified, only those ever in payroll jobs were included. Using the date of death, the cause of death was abstracted from death certificates at the Office of the Registrar General of Ontario.

Work histories: The Human Resources staff also supplied photocopies of job histories that were available. This amounted to providing copies of available change of rate or transfer slips, as well as hire slips and termination slips. These were not complete for every rate change but the Human Resources Manager considered them reasonably complete for inter-department changes. This writer had some uncertainties about the completeness of the work histories, and additional data were obtained through telephone communication and subsequent information forwarded in order to examine deaths among workers in the area of interest (HDI) in more detail. Detailed analyses were limited to this department.

RESULTS

MEN AND WOMEN IN THE STUDY POPULATION

Of the 132 names supplied, 115 were ever in payroll. Of these, two who were of unknown status at death and five who were vested but terminated before retirement, were excluded, leaving 108 deaths among those who were active, retired, or on long-term disability at the time of death. Of the 108, one died out of Ontario and the cause of death was not known. Death certificates were located for 103; of the other four, two death certificates could not be located and two were known to have drowned but the bodies were not recovered: they were coded as drownings, giving 105 for analysis. Of the 105, 88 were males and 17 were females: 52 (45 males, 7 females) were active; 17 (9 males, 8 females) were on long-term disability; and 36 (34 males, 2 females) were retirees at the time of death.

PROPORTIONS OF CAUSES OF DEATH COMPARED WITH GENERAL POPULATION OF ONTARIO

The comparison of proportions of causes of death in Celanese employees with those in the general Ontario population is shown in Table 1. As explained above, the expected deaths for a given cause (e.g. circulatory deaths) are obtained by multiplying the proportion or fraction of all deaths due to that cause in the general population of similar age by the total number of deaths in the Celanese study group. For example, the proportion of deaths due to circulatory disease in the male general population of the same age as the Celanese active deaths was 33.3%; thus, the expected number was the total number of deaths (45) times .333 = 15.0. The observed number was actually 18. The Proportional Mortality Ratio (PMR) is defined as the ratio of "observed/ expected" times 100. The PMR will be equal to 100 if the Celanese experience is the same as the Ontario average, less than 100 if fewer deaths due to the cause of interest were

experienced, and greater than 100 if the proportion is greater than the Ontario population. In this case, for circulatory disease, the PMR was 18/15.0 x 100 = 120, indicating that the proportion in Celanese active males was somewhat greater than the provincial experience. For all cancer, the situation was reversed, as the PMR was 75 or 25% lower than expected.

Table 1 gives observed, expected, and PMR values for males, (and observed and expected values only for females since the numbers are quite small). For all cancers, the proportions are about that expected for all males combined. One case of laryngeal cancer occurred. The proportion of lung cancer deaths was greater than expected, in both males and females dying while retirees/long-term disability. The proportions were increased (but <u>based on very small numbers)</u> for blood and lymph cancers (in retired females), bladder cancer (1 vs 0.4 in retired males; 1 vs 0.2 in active), and breast cancers. <u>No deaths from kidney cancer</u> (one of the cancers among the initial concerned employees) <u>nor from nasal cancer</u> (induced by PGE or C-8 in animals) were observed in the entire group.

Among non-malignant causes, circulatory deaths were slightly less than expected (94) in the retirees/ LTD group and about that expected overall, while the proportion of respiratory deaths was about that expected in males. The number of violent deaths was slightly above expectation in the active males. Deaths due to other causes occurred in very small numbers or not in excess.

<u>MORTALITY ACCORDING TO AREA OF CONCERN</u>

<u>HDI:</u> The concern had been expressed about the numbers of cancers among employees working in the HDI area. In addition, there is 1) unconfirmed evidence from one epidemiologic report among polyester workers of excess mortality from laryngeal and lung cancer; and 2) the presence of the animal carcinogen PGE in the Tire Yarn process. Thus, mortality patterns in the HDI work

areas were investigated further using work histories to the extent available, provided by the Company.

Work histories could be located for all but one woman; her work department (Filament Yarn) was finally located and communicated via the Human Resources Department. It is recognized that it takes some years for chemically induced tumours to appear; in other words, in examining the relationship between workplace exposures and death from cancer, it is reasonable to assume that work exposures in the years shortly before death are unlikely to have caused the tumour. Thus, jobs performed within five years of death were excluded from analysis.

The 105 workers were classified as to whether or not they had ever worked in HDI OR TIRE YARN PRODUCTION (excluding the 5 years before death). Foremen in Tire Yarn were also considered as "exposed". As can be seen (Table 2), the numbers of deaths among ever HDI workers was small: there were 11 (10.4%) of 105 deaths among ever-HDI, which is comparable to the proportions of the total workforce that was in HDI as noted above. Thus, 11 (7 males, 4 females) had ever worked in HDI production, while 94 (81 males, 13 females) had not.

In comparison to the general population of Ontario, the proportion of deaths due to all cancers was increased in ever HDI employees, but this is based on very few deaths (6 observed vs 3.7 expected in males and females combined); the number of cancer deaths was the same as that expected among never HDI employees. Of the 2 cancer deaths in HDI males, one was from laryngeal cancer (0.03 expected) and one was from lung cancer (0.5 expected). All four deaths in HDI females were from cancer, including 2 from lung cancer (0.4 expected), giving a total of 3 deaths (among males and females) from lung cancer (0.88 expected, PMR 341). The other deaths in HDI females were due to breast cancer and leukemia.

There was also a small increase of deaths due to lung cancer in never HDI males compared to the provincial expectation (10 observed, 6.8 expected, PMR 148). The other cancer deaths in non-HDI workers included bladder cancer (2 cases in males) and breast cancer (3 cases), digestive cancers (3 cases), and leukemia, lymphosarcoma, lymphoma not classified, prostate, brain, and cervical cancers, one each.

For non-cancer causes of death (circulatory disease, accidents), the proportions for both HDI and never HDI groups were similar to that expected.

Factors related to lung cancer and Celanese workers:

Lung cancer deserves more attention because 1) the proportion of deaths due to lung cancer was elevated in the Celanese population compared to Ontario (based on very small numbers) in the HDI group and to a lesser extent, the non-HDI group; and 2) lung cancer was the type of cancer that occurred in one of those first contacting the MOL Kingston office; and 3) the number of deaths from lung cancer observed in the French study was in excess of that expected (although not statistically significantly so, and the manufacturing process was somewhat different). No data to examine non-occupational factors such as smoking are available; the percentage of smokers among employees is not known. However, there is no reason to expect this to vary among different parts of the plant. Of note, none of the deaths from respiratory disease or from bladder cancer (both smoking-related) occurred among HDI workers.

Age and sex distribution: All but one of the 11 lung cancers in males were non-HDI. Table 3 shows that simple comparisons between HDI and non-HDI deaths cannot be made: no lung cancers occurred among female non-HDI workers; and all HDI lung cancer deaths occurred below age 65. Thus, there are no "non-exposed" female cases. However, within the 45-64 age stratum, 38% of

deaths among HDI workers compared to 15% of those among non-HDI workers were due to lung cancer (Table 3). Restricting the analysis to this age stratum, simply summing males and females yields a crude odds ratio for the association of ever in HDI and lung cancer of 3.5. To obtain a summary estimate of this association, adjusting for or "pooling" the data from two "strata" or subsets (in this case, males and females), the Mantel-Haenszel odds ratio was used (computed with Epistat computer program). The summary odds ratio, controlling for sex, is 4.1 (95% confidence interval 0.2, 83; p=0.35; Table 3). That is, lung cancer appeared three to four times more frequently among HDI workers, but this could be due to chance.

Non-HDI: Lung cancer was increased slightly (about 40% above provincial expectation) in the non-HDI deaths. An important fraction of the workforce worked in the Maintenance departments: the job histories indicated work as pipefitters, as well as mechanics, janitors, and so on. Asbestos, a lung carcinogen was known to be present at the plant in insulation. Thus, it seemed reasonable to examine the proportion of deaths among this group: workers were classified as ever maintenance if they had worked > 6 months in maintenance jobs, at least 5 years prior to death. As shown in Table 4, within this non-HDI group, the proportion of deaths due to lung cancer was somewhat increased among those ever in maintenance jobs, while it was the same as expected among the remaining non-HDI deaths. For one death in a maintenance worker coded on death certificate as lung cancer, the work history indicated work as a pipefitter; the insurance claim indicated "lung cancer (? mesothelioma)". The autopsy report was obtained, and provided pathological confirmation of mesothelioma. However, from the employment records obtained, this employee did not begin work at Celanese Canada until age 56, and died within seven years.

Moreover, it should be noted that mesothelioma associated with asbestos exposure typically appears 30 or more years after the

onset of exposure. For example, Browne (1983) illustrated using the workers studied by Selikoff, that of 175 mesotheliomas, all cases occurred more than 14 years after onset of exposure, with average latent period 30-34 years. Thus, it is most likely that prior, not current, work exposures may have been linked with this tumour in this maintenance worker.

The maintenance workers included a multitude of job titles including mechanic, machinist, janitor, millwright, pipefitter, and labourer. There were many maintenance "departments": as well as central maintenance, maintenance also included the instrument shop, electrical shop, machine shop, air conditioning, buildings and grounds, staple maintenance, HDI maintenance, and powerhouse maintenance. Workers moved back and forth between these maintenance departments but the work histories were not sufficiently complete to capture this. The Mantel-Haenszel odds ratio for the association of lung cancer and ever HDI, excluding maintenance workers was similar to that with all workers (5.1), and again, was not statistically significant ($p=0.30$).

<u>HDI Cases:</u> Table 5 summarizes the work histories of the HDI employees dying of laryngeal and lung cancer; the jobs in HDI included spinning, beaming, and bobbin recovery. Although the number of lung cancer cases (three) is small, relationships with duration of exposure or time since first in HDI were sought as evidence supporting a causal relation. The cases tended to have worked a short time in HDI (< 4 yrs for all three); there was no evidence of an increasing lung cancer PMR among those with > 3 years exposure (Table 6). When the relationship with time since first working in HDI was examined, no deaths occurred 20 years after first exposure (Table 7). This is not surprising given that the process began operation in 1966-68. One of the lung cancer cases occurred less than 10 years after first HDI exposure.

Did the HDI cases have other common exposures?: One female case spent the bulk (6 yrs) of time in C-50/ flex crew while the other female case spent 7 years in production services (Table 5). The male case spent 13 years as an operator in filament yarn, indicating no other long-term departments in common.

DISCUSSION

Of the 105 deaths among Celanese employees while active, retired, or on long-term disability, 11 occurred among ever-HDI workers, comparable to the proportion that this department represented of the entire plant. As anticipated, the results are inconclusive because of the small number of deaths among workers who worked one or more days in HDI, 5 or more years before death. The investigation was also limited because the HDI process has only been in operation for about 20 years.

The proportions of deaths due to cancer in all males was about that expected. The proportion due to lung cancer in males (11 observed vs 7.2 expected) represents about a 50% increase; no increase was observed among those not in maintenance or in HDI.

HDI: There was one death due to laryngeal cancer among HDI workers which is of interest given the findings of Hours et al (1986) but no conclusions can be drawn regarding a single case. We have observed 3 lung cancer deaths (0.88) expected among ever-HDI workers, including 2 deaths in young women 54 and 55 years of age at death. All worked for relatively short periods of time in HDI which is against the relationship being causal, and one of the three cases occurred less than 10 years since first in HDI (Tables 6, 7). Although the proportions were somewhat more than the Ontario average, the numbers were so small that this could have been a statistical fluke: assuming a Poisson distribution for observed deaths, there is a 12% probability of observing 3 or more deaths when 0.88 are expected.

No data about tobacco smoking, the most important cause of lung cancer, are available. However, the fact that no deaths from respiratory disease (bronchitis, emphysema) and bladder cancer (both of which are smoking-related) occurred among HDI workers but all occurred instead among the non-HDI group, suggests that they did not smoke more than the non-HDI workers.

There was no suggestion that the HDI lung cancer cases worked for extended periods in other departments in common.

Consistency: Unfortunately, no reports from similar polyester processes have been published. There is a Hoechst/ Celanese plant in North Carolina with an HDI process that began at a simi' . period (1969) but is much larger: about 1000 of the 2000 employees apparently being involved (Dr. Kevin Soden, personal communication, July 31, 1989). The medical director informed me that a mortality study of the plant is in progress: the names have been submitted to the National Death Index and to the Social Security Administration. He indicated his willingness to share any information that is obtained with the Ministry and the Millhaven plant.

Non-HDI: Lung cancer was also elevated by about 50% among non-HDI workers; subset analysis after examining the data (not declared in advance) suggested that this was found among those ever in maintenance occupations but not others. It is not clear to what extent workers in maintenance had occupational exposure to asbestos or other possible lung carcinogens. The insurance claim for one lung cancer death raised the possibility of mesothelioma in a pipefitter; the autopsy report provided pathological confirmation. However, as noted above, due to the brief period of time after starting work at the plant, it is very unlikely that work exposures at this plant can be implicated.

CONCLUSIONS

The following guidelines for the investigation of cancer clusters in the workplace suggested by Frumkin and Kantrowitz (1987) can be examined:

Step 1: Is a cancer cluster suspected? Answer: Yes, by the requestors, but no specific cancer type suspected in advance.

Step 2: Is there really an excess of cancer? Answer: No statistically significant cancer excess.

Step 3: Is any particular type of cancer over-represented? Answer: Possibly lung cancer in HDI (in women).

Step 4: Has sufficient latency elapsed? Answer: No.

Step 5: Are any confounders likely to have contributed? Answer: Although smoking status not known, other smoking-related diseases not found among HDI deaths.

Step 6: Is any particular job type over-represented among the cancer cases? Answer: Yes, HDI department but short duration of work argues against etiological role (jobs: spining, beaming, bobbin recovery).

Step 7: Can any carcinogenic job exposures be identified? Answer: Yes, PGE induced nasal cancers in animals. No other compounds in HDI known to be carcinogenic.

In summary, among ever HDI workers, 3 cases of lung cancer were observed vs 0.88 expected including 2 deaths in young women (0.4 expected) both about 55 years of age at death. It is not surprising that based on such small numbers, this excess or the odds ratio comparing HDI to non-HDI are not "statistically significant". The short duration of exposure of the cases argues against the association of lung cancer with HDI exposure being causal. While it is recognized that this study is limited by not having examined cancer incidence, because of the inadequate period of follow-up that has elapsed since start-up of the operation and the small number of HDI workers, the author suspects that with the data available, it will not be possible at this time to give a definitive answer to the question of lung (or other) cancer risk among HDI workers at Celanese Canada. It is doubtful that any further study <u>at this time</u>, including cancer incidence, will provide definitive information. There is no suggestion of an excess from other cancers among HDI workers.

RECOMMENDATIONS:

Regarding HDI:

1. The mortality or cancer incidence experience could be examined among HDI workers with longer duration of exposure and greater than 20 years since first exposure. As the process did not start until 1966-1968, this situation is unlikely to exist for another 5-10 years. A case-control design could be considered.
2. In order to gain more information at the present time, it is preferable to examine workers exposed to the same process at a different location, to see if the findings, which are only suggestive here and cannot be considered causal, are observed elsewhere. The mortality experience of a much larger group engaged in an apparently similar process will be available from the study underway at the Hoechst/ Celanese plant in North Carolina. It is recommended that the Joint Health and Safety Committee (JHSC) obtain the data when the study is completed. The Health Studies Service is available to work with the JHSC in interpreting the findings of the study.
3. As phenyl glycidyl ether has been demonstrated to be an animal carcinogen, exposure should be monitored to ensure it remains as low as possible; the results of air sampling conducted in recent years show exposure to be quite low. Ongoing measurements should be conducted to ensure that this situation continues.

Regarding asbestos:

4. The JHSC should ensure that there is no ongoing asbestos exposure at this time.

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TABLE 1
CAUSES OF DEATH OCCURRING AMONG CELANESE EMPLOYEES
COMPARED TO ONTARIO POPULATION

		MALES			FEMALES	
CAUSE	STATUS	OBS	EXP	PMR	OBS	EXP
All causes	R + L	43			10	
	A	45			7	
All cancers	R + L	14	12.2	115	6	4.4
	A	7	9.4	75	3	2.2
Digestive Cancers (ICD 150-159)	R + L	3	3.6	82	0	1.0
	A	0	2.6	0	0	0.4
Laryngeal Cancer	R + L	1	0.2	562	0	0.01
	A	0	0.1	0	0	0.0
Lung Cancer	R + L	7	4.3	162	2	0.8
	A	4	2.9	138	0	0.2
Blood/ Lymph Cancer (ICD 200-208)	R + L	1	1.0	100	2	0.3
	A	1	1.2	83	0	0.3
Breast Cancer	R + L	-			2	1.2
	A	-			2	0.6
Circulatory Disease (Heart & Stroke)	R + L	19	20.3	94	1	3.1
	A	18	15.0	120	1	1.1
Respiratory Diseases	R + L	4	2.9	137	2	0.4
	A	1	1.5	67	0	0.3
Violents/Accidents	R + L	2	2.4	83	1	0.7
	A	17	13.5	126	2	2.2

Key: Status at Death: Retired or Long-term Disability (R+L)
Active (A)
PMR=Proportional Mortality Ratio; OBS=Observed;EXP=Expected
NOTE: In this and subsequent tables, expected numbers have been rounded off.

TABLE 2: COMPARISON OF CAUSES OF DEATH AMONG CELANESE WORKERS TO THE ONTARIO POPULATION ACCORDING TO WHETHER EMPLOYED IN THE HDI (TIRE YARN) DEPARTMENT

		MALES		FEMALES	TOTAL	
CAUSE	STATUS	OBS/ EXP	PMR	OBS/ EXP	OBS	PMR*
All causes	HDI	7		4	11	
	Never	81		13	94	
All cancers	HDI	2/ 1.6	122	4/ 2.1	6	161
	Never	19/ 19.9	95	5/ 4.5	24	98
Digestive Cancer (ICD 150-159)	HDI	0/ 0.4	0	0/ 0.4	0	0
	Never	3/ 5.8	52	0/ 1.0	3	44
Lung Cancer	HDI	1/ 0.5	208	2/ 0.4	3	341
	Never	10/ 6.8	148	0/ 0.5	10	137
Breast Cancer	HDI	--		1/ 0.6		
	Never	--		3/ 1.2		
Blood & Lymph Cancer (200-208)	HDI	0/ 0.2	0	1/ 0.1	1	
	Never	2/ 2.0	101	1/ 0.5	3	123
Circulatory Disease	HDI	3/ 2.4	127	0/ 0.9	3	93
	Never	34/33.0	103	2/ 3.4	36	99
Respiratory Disease	HDI	0/ 0.2	0	0/ 0.1	0	0
	Never	5/ 4.2	119	2/ 0.6	7	147
Digestive Disease	HDI	0/ 0.4	0	0/ 0.2	0	0
	Never	4/ 3.7	107	1/ 0.6	5	116
Violence/ Accidents	HDI	2/ 1.8	111	0/ 0.3	2	83
	Never	17/14.1	121	3/ 2.5	20	121

Key: Status: HDI = Ever worked in HDI production
Never = never worked in HDI production area
PMR=Proportional mortality ratio; OBS=observed; EXP=expected
* = PMRs calculated for causes with 3 or more deaths

TABLE 3: THE AGE AND SEX DISTRIBUTION OF DEATHS BETWEEN HDI AND NON-HDI WORKERS

	Males		Females		All		
	Lung Cancer	Other Causes	Lung Cancer	Other Causes	Lung Cancer	Other Causes	Total
Age at Death Less than 45:							
HDI	0	3	0	0		3	3
Never HDI	0	17	0	5		22	22
Total	0	20	0	5		25	25
Age at Death 45-64:							
HDI	1(25%)	3(75%)	2(50%)	2(50%)	3 (38%)	5 (62%)	8
Never HDI	6(17%)	30(83%)	0(0%)	5(100%)	6 (15%)	35(85%)	41
Total	7	33	2	7	9	40	49
Age at Death 65 or More:							
HDI	0	0	0	0	0	0	0
Never HDI	4(14%)	24(86%)	0	3(100%)	4	27	31
Total	4	24	0	3	4	27	31

Ages 45-64: Mantel-Haenszel Odds Ratio for the association of ever in HDI and lung cancer = 4.1 (95% confidence interval 0.2, 83; p=0.35)

NOTE: Type size has been reduced to accommodate table width.

TABLE 4

COMPARISON OF LUNG CANCER DEATHS AMONG HDI, MAINTENANCE, AND OTHER EMPLOYEES TO ONTARIO AVERAGE

		MALES		FEMALES
CAUSE	DEPT	OBS/ EXP	PMR	OBS/ EXP
All causes	HDI	7		4
	Maint	31		0
	Other	50		13
All cancers	HDI	2/ 1.6	122	4/ 2.1
	Maint	9/ 8.8	103	-
	Other	10/ 11.2	90	5/ 4.5
Lung cancer	HDI	1/ 0.5	208	2/ 0.4 (502)
	Maint	6/ 3.2	189	-
	Other	4/ 3.6	112	0/ 0.5

Key to Department: HDI = ever in HDI 5 years before death
Maint = > 6 months in maintenance 5 years before death

TABLE 5

WORK HISTORIES OF EVER HDI EMPLOYEES DYING OF LARYNGEAL AND LUNG CANCER

A) Laryngeal cancer. Male. Died 1983, age 51.
Exposure in Tire Yarn 12.2 years (10.3 yrs accumulated prior to 5 yrs before death). Time since first in Tire Yarn: 15 yrs

FILAMENT YARN (draw twist/ spinning operator) 1957-1968
TIRE YARN (spin draw) April 1968-June 1980
PRODUCTION SERVICES (bobbin recovery) 1981-1982
C-50 (Yarn rewind operator) 1983

B) Lung cancer. Male. Died 1987, age 56.
Exposure in Tire Yarn 0.4 yrs. Time since first in Tire Yarn: < 15 yrs

POLYMER (helper) April 1957-December 1958.
FILAMENT YARN (draw twist operator) 1958-1971
Janitor 1971-1975
TIRE YARN (spinning serviceman) March 31, 1975-August 24, 1975
STAPLE FIBRE/PROD'N SERVICES (pillow helper) August 1975- November 1982

C) Lung cancer. Female. Died 1987, age 55.
Exposure in Tire Yarn 5 months (0.4 yr) prior to 5 yr prior to death. Time since first in Tire Yarn: 11 yrs.

PRODUCTION SERVICES (bobbin recovery) March 1974
STAPLE (winding operator) April 1974
C-50 (process operator) April-October 1974
PRODUCTION SERVICES (bobbin recovery) October 1974-April 1975
C-50 (operator) April 1975-April 1976
TIRE YARN (bobbin recovery; beaming) April 1976-August 1976
C-50/ Flex crew 1979-1985
TIRE YARN (beaming) May 7-29, 1985

D) Lung Cancer. Female. Died 1985, age 54.
Exposure in Tire Yarn 7.7 years total (3.8 yr prior to 5 yrs prior to death). Time since first in Tire Yarn: < 10 yrs

PRODUCTION SERVICES (bobbin recovery) Sept-Dec 1968
SERVICES (packing, insp, bobbin recovery) Jan 1969-Dec 1976
TIRE YARN (bobbin recovery) June 1976-October 1976
TIRE YARN (beaming) October 1976-Feb 1984

TABLE 6

ANALYSIS OF DEATHS IN EVER HDI EMPLOYEES

ACCORDING TO DURATION OF WORK IN HDI

	Years in HDI							
	Less than 3				3 or more			
	Males	Females	All		Males	Females	All	
Cause of death	O/E	O/E	O/E	PMR	O/E	O/E	O/E	PMR
All causes	4	2	6		3	2	5	
All cancers	1/0.84	2/1.01	3/1.85	162	1/0.79	2/1.08	3/1.87	160
Lung cancer	1/0.20	1/0.18	2/0.38	526	0/0.28	1/0.22	1/0.50	200
Circulatory	1/1.02	0/0.46	1/1.48	66	2/1.34	0/0.42	2/1.76	114

KEY: O = Observed

E = Expected

PMR = Proportional mortality ratio = observed/ expected x 100

(percentage of expected that was observed)

NOTE: Type size has been reduced to accommodate table width.

TABLE 7

PROPORTIONAL MORTALITY ANALYSIS OF MDI DEATHS

ACCORDING TO TIME SINCE FIRST WORKED IN MDI

	Time since first in MDI (years)									
	< 10				10-19				20 or more	
Cause	**Males**	**Females**	**All**		**Males**	**Females**	**All**		**All**	
of death	**O/E**	**O/E**	**O/E**	**PMR**	**O/E**	**O/E**	**O/E**	**PMR**	**O**	**PMR**
All causes	4	2	6		3	2	5		0	0
All cancers	0/0.74	2/1.03	2/1.74	115	2/0.89	2/1.06	4/1.95	205	0	0
Lung cancer	0/0.16	1/0.18	1/0.34	294	1/0.32	1/0.22	2/0.54	370	0	0
Circulatory diseases	2/1.12	0/.42	2/1.54	130	1/1.24	0/0.46	1/1.70	59	0	0

KEY: O = Observed

E = Expected

PMR = observed/ expected x 100

NOTE: Text size has been reduced to accommodate table width.